

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
19 February 2004 (19.02.2004)

PCT

(10) International Publication Number
WO 2004/014417 A3

(51) International Patent Classification⁷: **A61K 39/095**,
C12N 1/21, A61P 37/04, A61K 39/102

(21) International Application Number:
PCT/EP2003/008568

(22) International Filing Date: 31 July 2003 (31.07.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

0218037.0	2 August 2002 (02.08.2002)	GB
0218036.2	2 August 2002 (02.08.2002)	GB
0218035.4	2 August 2002 (02.08.2002)	GB
0218051.1	2 August 2002 (02.08.2002)	GB
0220197.8	30 August 2002 (30.08.2002)	GB
0220199.4	30 August 2002 (30.08.2002)	GB
0225524.8	1 November 2002 (01.11.2002)	GB
0225531.3	1 November 2002 (01.11.2002)	GB
0230164.6	24 December 2002 (24.12.2002)	GB
0230168.7	24 December 2002 (24.12.2002)	GB
0230170.3	24 December 2002 (24.12.2002)	GB
0305028.3	5 March 2003 (05.03.2003)	GB

(71) Applicant (for all designated States except US): **GLAXOSMITHKLINE BIOLOGICALS SA** [BE/BE]; Rue de l'Institut 89, B-1330 Rixensart (BE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BIEMANS, Ralph** [BE/BE]; GlaxoSmithKline Biologicals S.A., Rue de l'Institut 89, B-1330 Rixensart (BE). **DENOEL, Philippe** [BE/BE]; GlaxoSmithKline Biologicals S.A., Rue de l'Institut 89, B-1330 Rixensart (BE). **FERON, Christiane** [BE/BE]; GlaxoSmithKline Biologicals S.A., Rue de l'Institut 89, B-1330 Rixensart (BE). **GORAJ, Karine** [BE/BE]; GlaxoSmithKline Biologicals S.A., Rue de

l'Institut 89, B-1330 Rixensart (BE). **POOLMAN, Jan** [NL/BE]; GlaxoSmithKline Biologicals S.A., Rue de l'Institut 89, B-1330 Rixensart (BE). **WEYNANTS, Vincent** [BE/BE]; GlaxoSmithKline Biologicals S.A., Rue de l'Institut 89, B-1330 Rixensart (BE).

(74) Agent: **LUBIENSKI, Michael, John**; GlaxoSmithKline, CIP (CN925.1), 980 Great West Road, Brentford, Middlesex TW8 9GS (GB).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
22 July 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **VACCINE COMPOSITIONS COMPRISING L2 AND/OR L3 IMMUNOTYPE LIPOOLIGOSACCHARIDES FROM LGTB- NEISSERIA MINIGITIDIS**

(57) Abstract: The present invention relates to the field of neisserial vaccine compositions, their manufacture, and the use of such compositions in medicine. More particularly it relates to processes of making novel engineered meningococcal strains which are more suitable for the production of neisserial, in particular meningococcal, outer-membrane vesicle (or bleb) vaccines. Advantageous processes and vaccine products are also described based on the use of novel LOS subunit or meningococcal outer-membrane vesicle (or bleb) vaccines which have been rendered safer and/or more effective for use in human subjects. In particular combinations of gene downregulations are described such as PorA & OpA, PorA and OpC, OpA and OpC, and PorA and OpA and OpC. Alternatively, or in addition, lgtB⁻ is shown to be an optimal mutation for effectively and safely using L3 and/or L2 LOS in Neisseria vaccine compositions. Bleb vaccines derived from lgtB⁻ and capsular polysaccharide deficient meningococcal mutants are further described; as are advantageous methods of making bleb preparations where LOS is to be retained as an important antigen.

WO 2004/014417 A3